UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/035,427	03/22/93	ANDERSON	182P102

ALLEN, M

18N2/0223

EXAMINER

GENENTECH, INC.
GINGER R. DREGER
460 POINT SAN BRUNO BOULEVARD
SOUTH SAN FRANCISCO, CA 94080

ART UNIT	PAPER NUMBER
1812	9

DATE MAILED: 02/23/94

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 11/26/93 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1, 11-12, 15-17, 24-28, 30-31, 58-60, 62-65, 67-73 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☒ Claims 2-10, 13-14, 18-23, 29, 32-57, 61, 66 have been cancelled.

3. ☒ Claims 1, 30-31, 58, 60, 62-65, 67-71 are allowed.

4. ☒ Claims 11-12, 15-17, 24-28, 59, 72-73 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

Claims 18-23, 29, 61, and 66 have been canceled. Claims 2-10, 13-14, and 32-57 have been canceled previously. Claims 1, 11-12, 15-17, 24-28, 30-31, 58-60, 62-65, and 67-73 are under consideration by the Examiner.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The provisional rejection of claims 1, 11-12, 19-31, and 58-73 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 9-27, 33, 35, and 37 of copending application Serial No. 07/894,213 has been withdrawn due to the filing of a proper terminal disclaimer, Paper No. 7.

The Keyt declaration under 37 C.F.R. § 1.132 filed 10 December 1993 is sufficient to overcome the rejection of claims 1, 11, and 58-59 based upon Goeddel et al. (U.S. Patent No. 4,766,075).

The declaration establishes that the t-PA variant N250 had a different plasma clearance rate and that t-PA variants N64S66 and N64T66 would be reasonably expected to have plasma clearance rates different from wild-type t-PA.

Claims 59, 72, and 73 are directed to an invention not patentably distinct from claims 12-17 of commonly assigned 07/841,698 for the reasons set forth below in the obviousness type double patenting rejections.

The instant application has a Genentech Attorney Docket No. 488P1C2 although it appears from Patent and Trademark Office records that the application is presently assigned to the inventors. It is noted that application Serial No. 07/824,740 is assigned to Genentech and that the instant application is a continuation of this application. Application Serial No. 07/841,698 is assigned to Genentech. MPEP 306 states that in the case of continuation a prior assignment recorded against the original application is applied to the continuation application. As such, the facts set forth above are deemed to be sufficient evidence for a presumption that the instant and 07/841,698 applications are currently commonly owned. It is noted that there are no inventors in common.

Commonly assigned 07/841,698, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. § 103 if the commonly assigned case qualifies as prior art under 35 U.S.C. § 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was

made. In order for the examiner to resolve this issue, the assignee is required under 37 C.F.R. § 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application. A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. § 103 based upon the commonly assigned case as a reference under 35 U.S.C. § 102(f) or (g).

Claim 59 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-15 of copending application Serial No. 07/841,698. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of both applications are drawn to methods of treating thrombolytic conditions by administering t-PA variants with novel glycosylation sites. The t-PA variants administered overlap although the claims differ in scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 72 and 73 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-17 of copending application Serial No. 07/841,698 in view of Larsen et al. (WO 87/04722). Claim 72 is drawn to a method of treating thrombolytic conditions by administering t-PA variants having a novel glycosylation site at amino acid 103 and removal of a glycosylation site at 117-119, 184-186, 218-220, and/or 448-450. Claim 73 is drawn to a method of treating thrombolytic conditions by administering t-PA variants having a novel glycosylation site at amino acid 103, substitution of alanine at amino acid positions 296-299, and removal of a glycosylation site at 117-119, 184-186, 218-220, and/or 448-450. Copending 07/841,698 claims methods of treating thrombolytic conditions by administering t-PA variants having a novel glycosylation site at amino acid 103 as well as a novel glycosylation site at amino acid 103 with a further substitution of alanine at amino acid positions 296-299. Larsen et al. teaches removal of a glycosylation site at 117-119, 184-186, 218-220, and/or 448-450. It would have been obvious to take the copending 07/841,698 variants and further modify them according to Larsen et al. (WO 87/04722) and then use them in methods of treatment. One would have been motivated to combine known mutations for their known and useful properties in order to develop improved pharmaceutical compositions for treatment.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the t-PA variants administered overlap although the claims differ in scope.

This is a provisional obviousness-type double patenting rejection.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.78(d).

Applicant is again requested to bring to the attention of the Examiner any other co-pending applications containing similar subject matter.

Claims 15, 17, and 28 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited as outlined below. See M.P.E.P. §§ 706.03(n) and 706.03(z).

The specification enables only deletion of amino acids 1-44 of the finger region. It would constitute undue experimentation to determine other deletions in the finger region that would result in a functional protein. (See claim 15.)

The specification enables only modification of the glycosylation site at amino acid 184 of t-PA via amino acid substitution to prevent glycosylation. (See for example claim 63.) It would constitute undue experimentation to determine what

levels of carbohydrate would remain functional by any other method and how to produce the so-modified t-PA's. (See claim 17.)

The specification enables only substitution at amino acid positions 275 and 277 to render them resistant to enzymatic cleavage. It would constitute undue experimentation to determine other modifications in these sites would result in a functional protein with the requisite resistance to enzymatic cleavage. (See claim 28.)

Claims 11-12, 16, and 24-27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is indefinite in referring to amino acid position 50. There is no antecedent basis for this position in claim 1.

Claim 16 is confusing in reciting "comprising natural t-PA." The variant of claim 1 is not natural t-PA. It appears that this claim should recite something approximating "variant of claim 15 further comprising deletion of amino acids 1-44."

Claims 24 and 26 are indefinite in depending upon canceled claim 23.

The Gething et al. reference (U.S. Patent No. 5,041,376) has not been applied to the claims of the instant application.

Gething et al. discloses proteins having supernumerary N-linked oligosaccharide side chains which shield functional sites or epitopes and genes encoding them. Substitution at amino acid position 67 of t-PA is specifically exemplified. This patent is not considered prior art to the instant application. The instant claims are not entitled to benefit of the 07/196,909 parent filing date (20 May 1988) because the scope of the present claims is not disclosed nor enabled therein. For example, mutation at amino acid positions 103 and 105 are not specifically disclosed. (Each claim is given benefit of only the filing date in which the full scope of the claim is described and enabled.) However, the disclosure of the 07/196,909 application is deemed to be sufficient to antedate the Gething et al. reference because it was filed in the United States prior to the filing date of the Gething et al. application and reduces to practice the specific N67 t-PA embodiment disclosed by Gething et al. It is noted that the Gething et al. patent claims are drawn to a method for shielding sites rather than the t-PA variant, pharmaceutical composition, or method of treatment as claimed in the instant application.

Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is (703) 308-0666.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

ROBERT J. HILL, JR.
SUPERVISORY PATENT EXAMINER
GROUP 1800